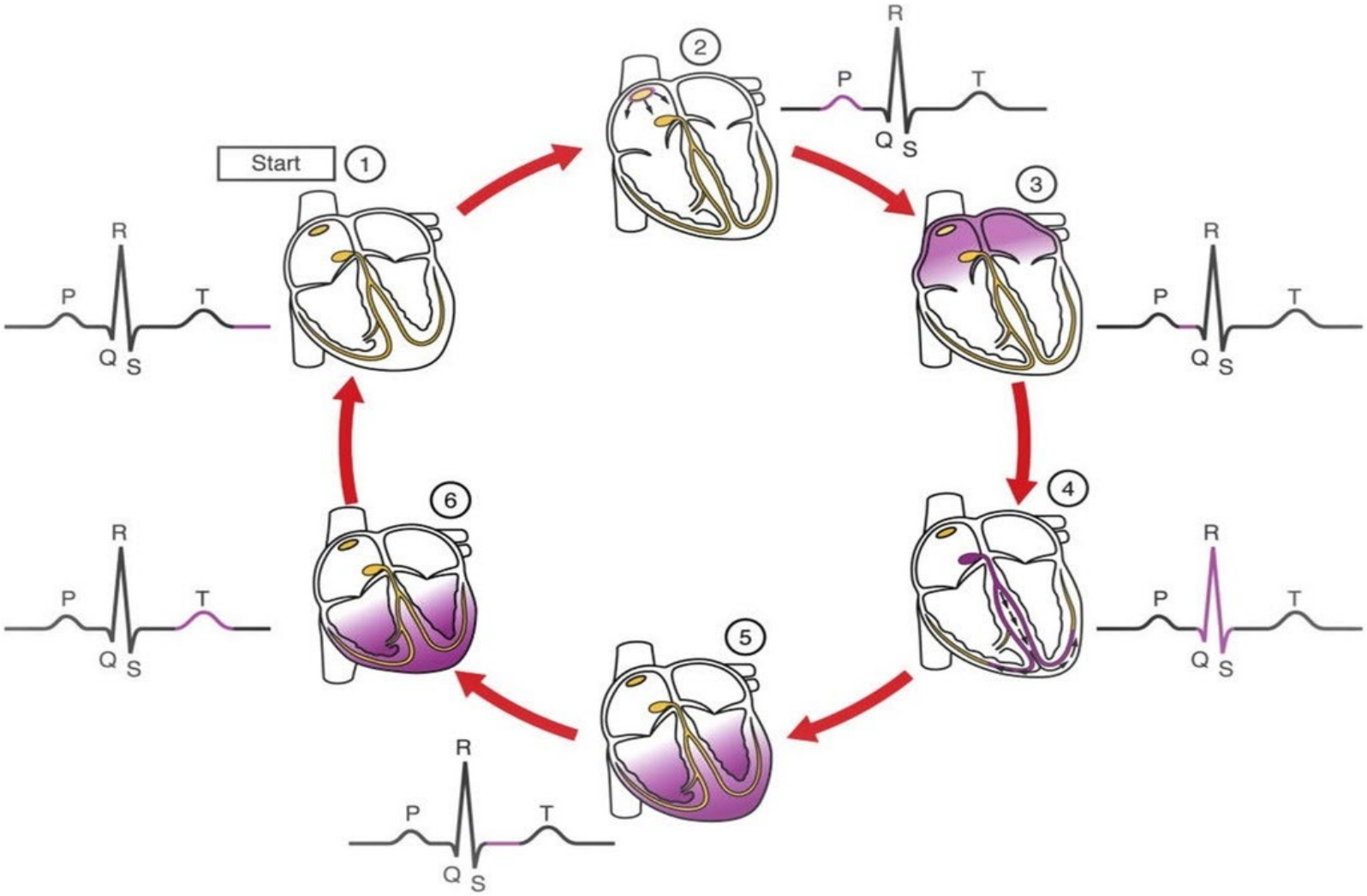
The Cardiac Cycle



Cardiac Cycle

- Cardiac cycle - one complete contraction and relaxation of all four chambers of the heart (0.8 sec)
- Atrial systole (atrial contraction) occurs during ventricles diastole (ventricle relaxation)
- Ventricular systole (ventricle contraction) occurs during atrial diastole (atrial relaxation)
- Quiescent period occurs when all four chambers are relaxed at same time (diastolic phases)

Timing of Cardiac Cycle

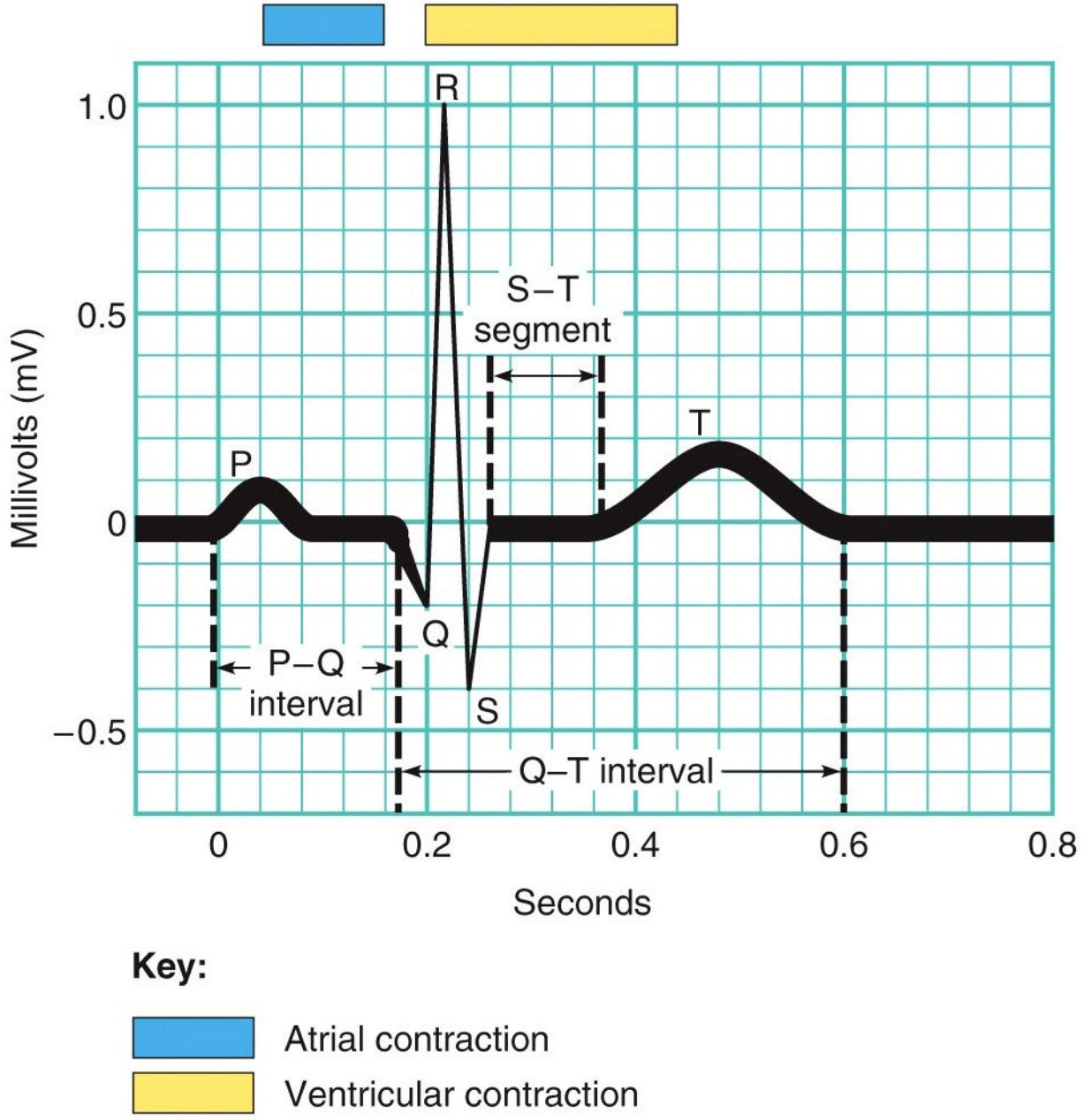
In a resting person

–atrial systole last about 0.1 sec

–ventricular systole about 0.3 sec

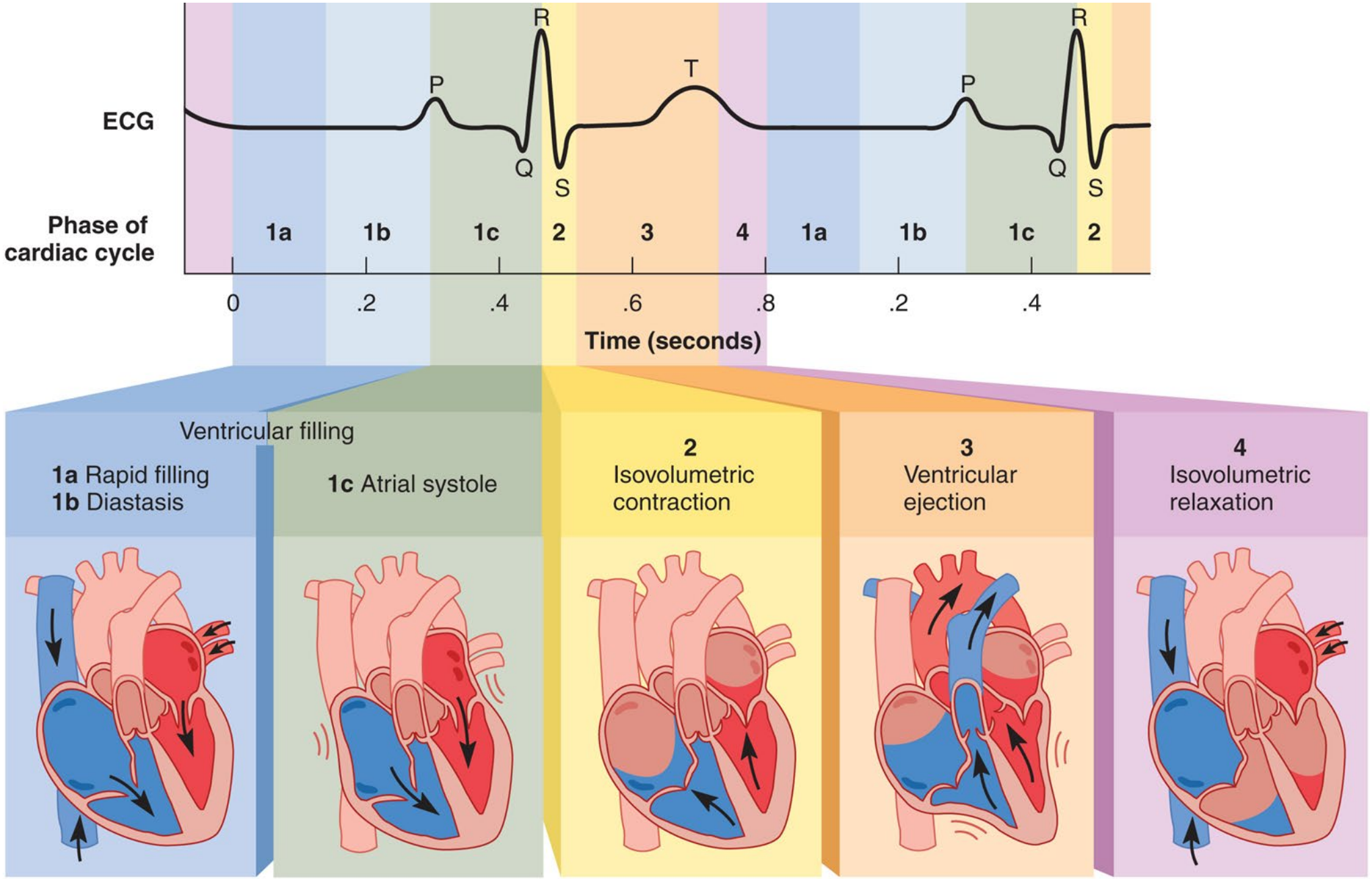
–quiescent period, when all four chambers are in diastole, 0.4 sec

- Total duration of the cardiac cycle is therefore 0.8 sec // 75 bpm
- To analyze these events which occur in all four chambers, it is best to follow the events that occur in a single chamber.
- We will focus on events which occur in the left ventricle.
- The left and right ventricle “must” receive and eject the same volume of blood.


R
1.0
0.5
S–T
segment
T
P
0
Millivolts (mV)
Q
P–Q
interval
S
–0.5
Q–T interval
0
0.2
0.4
0.6
0.8
Seconds
Key:
Atrial contraction
Ventricular contraction

Phases of Cardiac Cycle

Ventricles start to fill before atria contract!



Events of Ventricular Filling (1 of 3)

- Blood moves from a high pressure into an aera of low pressure.
- As the ventricles relaxes, the pressure in atria is greater than ventricular pressure and this will cause the AV valves to open.

Ventricular pressure drops below pressure in atria

AV valves open and blood flows into the ventricles

Events of Ventricular Filling

Ventricular filling occurs in three phases:

Rapid ventricular filling - first one-third /// blood enters very quickly / passive and occurs before atrial systole begins

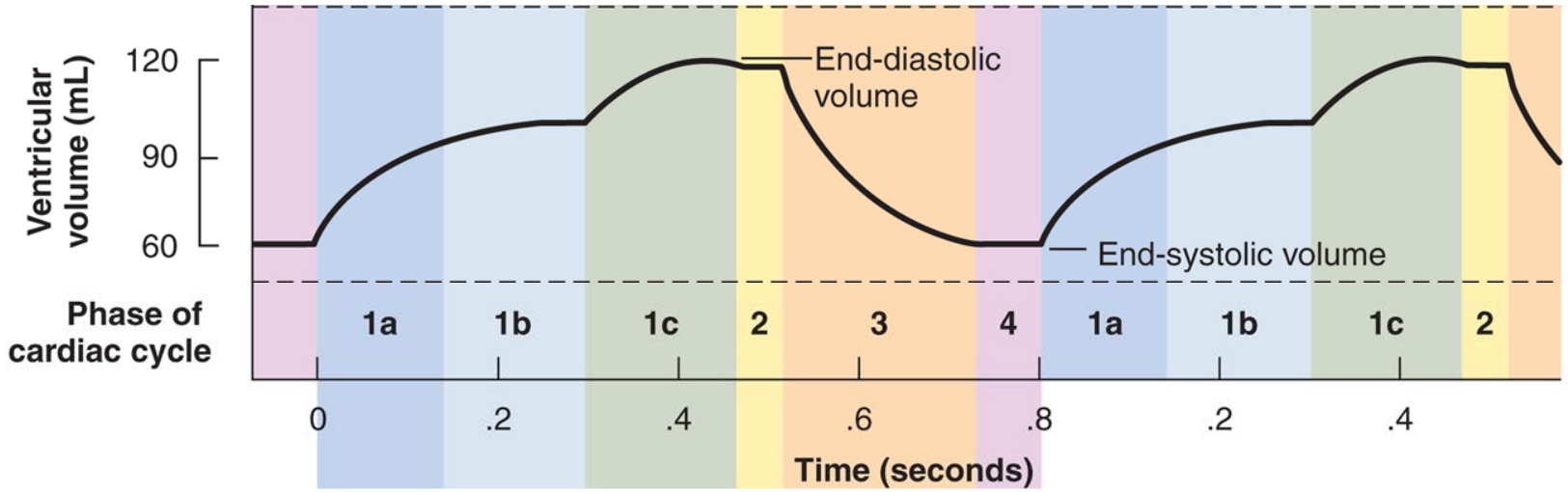
Diastole continues in atria - second one-third // marked by slower filling of ventricle

Now P wave occurs (depolarization occurs) /// this starts atrial systole –

Final one-third filling of ventricle occurs with the atria contraction

> What is the clinical significance for a patient with atrial fibrillation (Afib)?

End-Diastolic VS End Systolic Volumes
Volume Changes Between the Two Iso-Volumetric Phases



End-diastolic volume occurs when ventricles stop filling with blood (EDV)

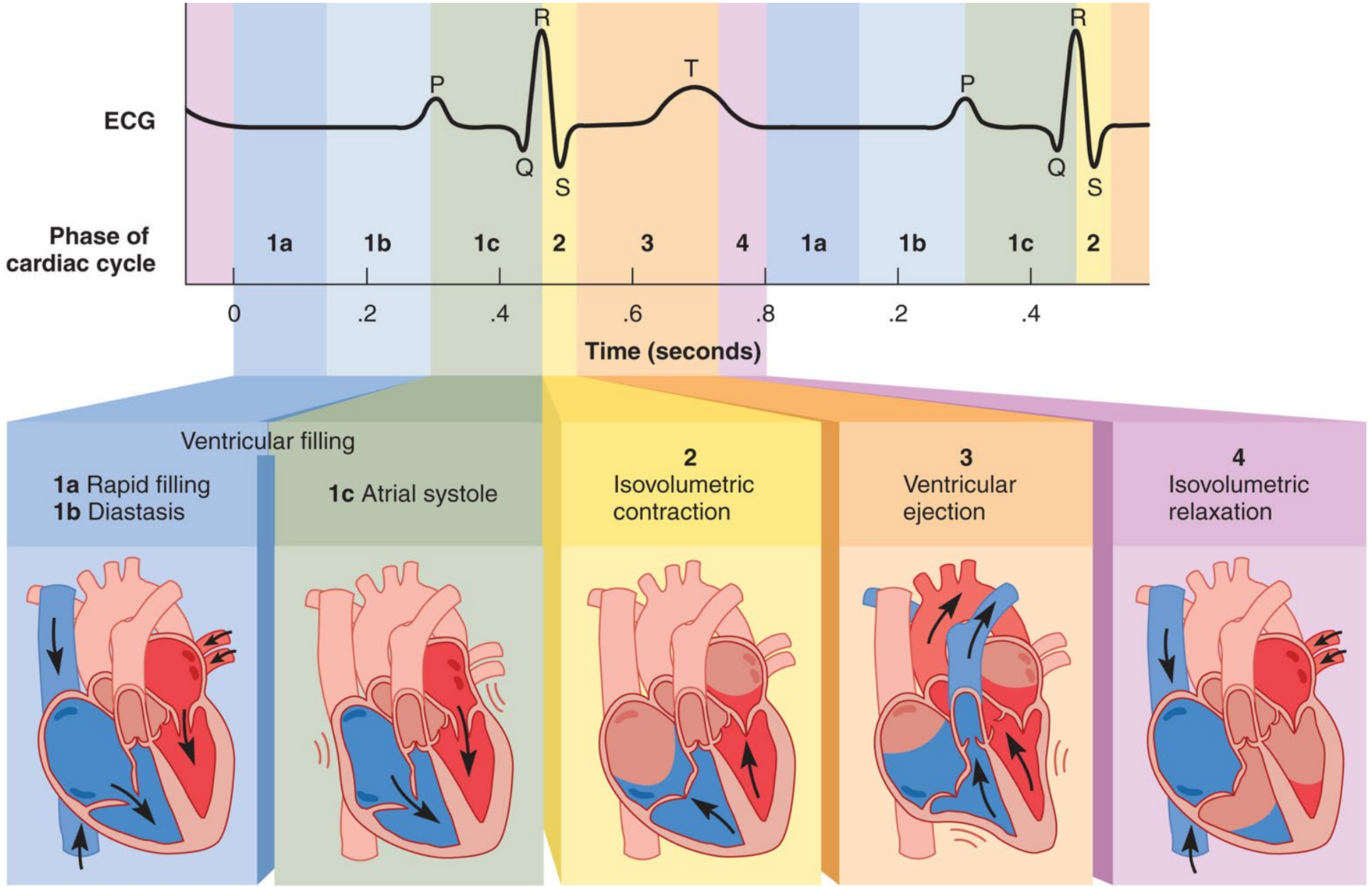
This is the amount of blood contained in ventricles at the end of ventricular filling

Same volume must be in both right and left ventricles // if different then it is called heart failure!

EDV is 130 mL of blood in each ventricle at end of ventricular diastole while in a resting state

ESV is 60 ml of blood and stroke volume is 70 ml

Events of Ventricular Filling



Events of Iso-volumetric Contraction

Iso-volumetric describes condition in ventricle when semilunar valve and atrial-ventricular valve are both closed

During isovolumetric contraction, the atria repolarize, and they are in diastole // remain in diastole for the rest of the cardiac cycle

Now ventricles depolarize (enter period of systole - contraction)

- –this initiates the QRS complex
- –depolarization of ventricle and ventricles contract
- –pressure in ventricles start to increase

AV valves close as ventricular blood pressure increases // forcing blood to surge back against the AV cusps (this causes the first heart sound, S_1) and closes of AV valves

Semilunar valves are still closed from previous cycle /// therefore – both AV valves and semilunar valves are both closed!

This is isovolumic contraction!

Events of Iso-volumetric Contraction

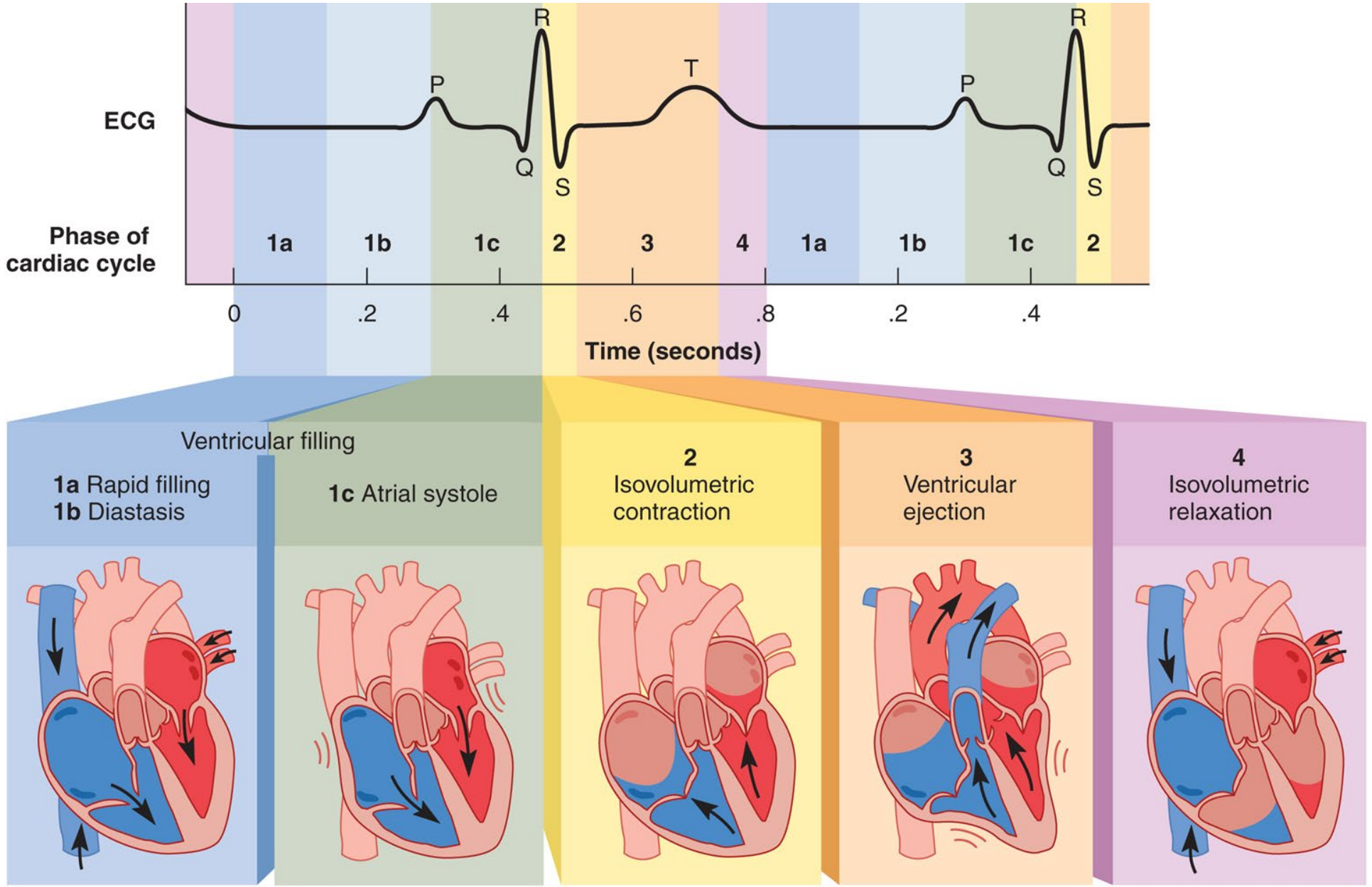
As you continue in the ‘isovolumetric’ contraction phase, ventricle is contracting but no blood is ejected because AV and semilunar values are BOTH STILL CLOSED

Semilunar valves are closed because pressure in the aorta (80 mm Hg) and in pulmonary trunk (10 mm Hg) is still greater than in the pressure in the two ventricles

Wall all four valves closed, the blood cannot go anywhere // This results in rapid increase in ventricular pressure

Eventually, ventricular pressure exceeds pressure in aortic arch and pulmonary truck (this pressure is called after-load) and now the semilunar values opens, and blood is ejected from the ventricles.

Events of Iso-volumetric Contraction



Events of Ventricular Ejection

Ejection of blood begins when the ventricular pressure exceeds afterload in pulmonary trunk and aorta and forces semilunar valves open

Pressure peaks in left ventricle at about 120 mm Hg and 25 mm Hg in the right

Blood ejected out of each ventricle rapidly at first – rapid ejection

Followed by slower rate of blood ejection because reduced pressure – reduced ejection

Ventricular ejections last about 200 – 250 msec

This corresponds to the plateau phase of the cardiocyte action potential

(See next slide)

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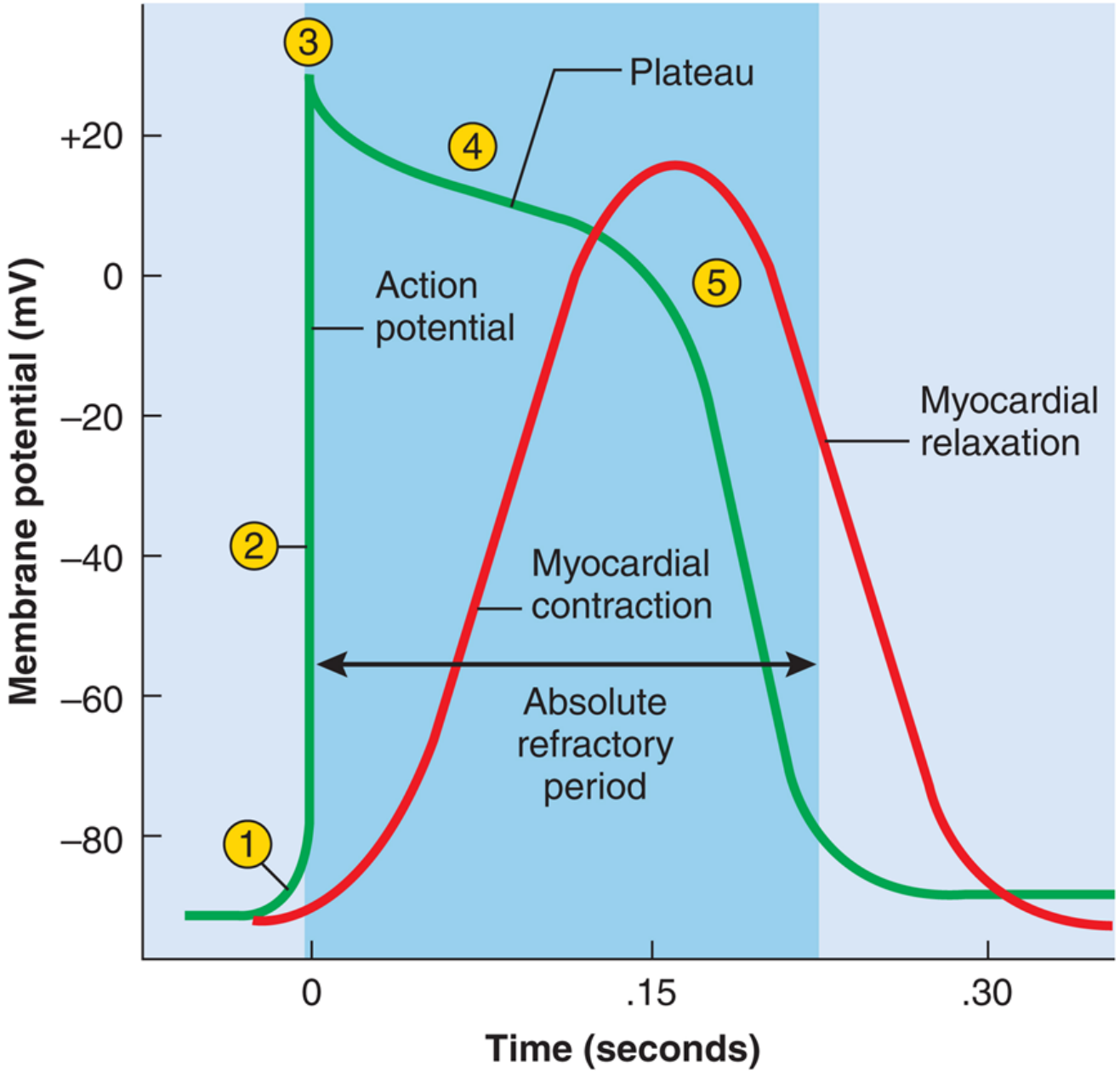


1. Voltage-gated Na^+ channels open.
2. Na^+ inflow depolarizes the membrane and triggers the opening of still more Na^+ channels, creating a positive feedback cycle and a rapidly rising membrane voltage.
3. Na^+ channels close when the cell depolarizes, and the voltage peaks at nearly +30 mV.
4. Ca^{2+} entering through slow Ca^{2+} channels prolongs depolarization of membrane, creating a plateau. Plateau falls slightly because of some K^+ leakage, but most K^+ channels remain closed until end of plateau.
5. Ca^{2+} channels close and Ca^{2+} is transported out of cell. K^+ channels open, and rapid K^+ outflow returns membrane to its resting potential.

Events of Ventricular Ejection

Stroke volume (SV) = 70 mL of blood from the 130 mL of blood in each ventricle (resting state volumes)

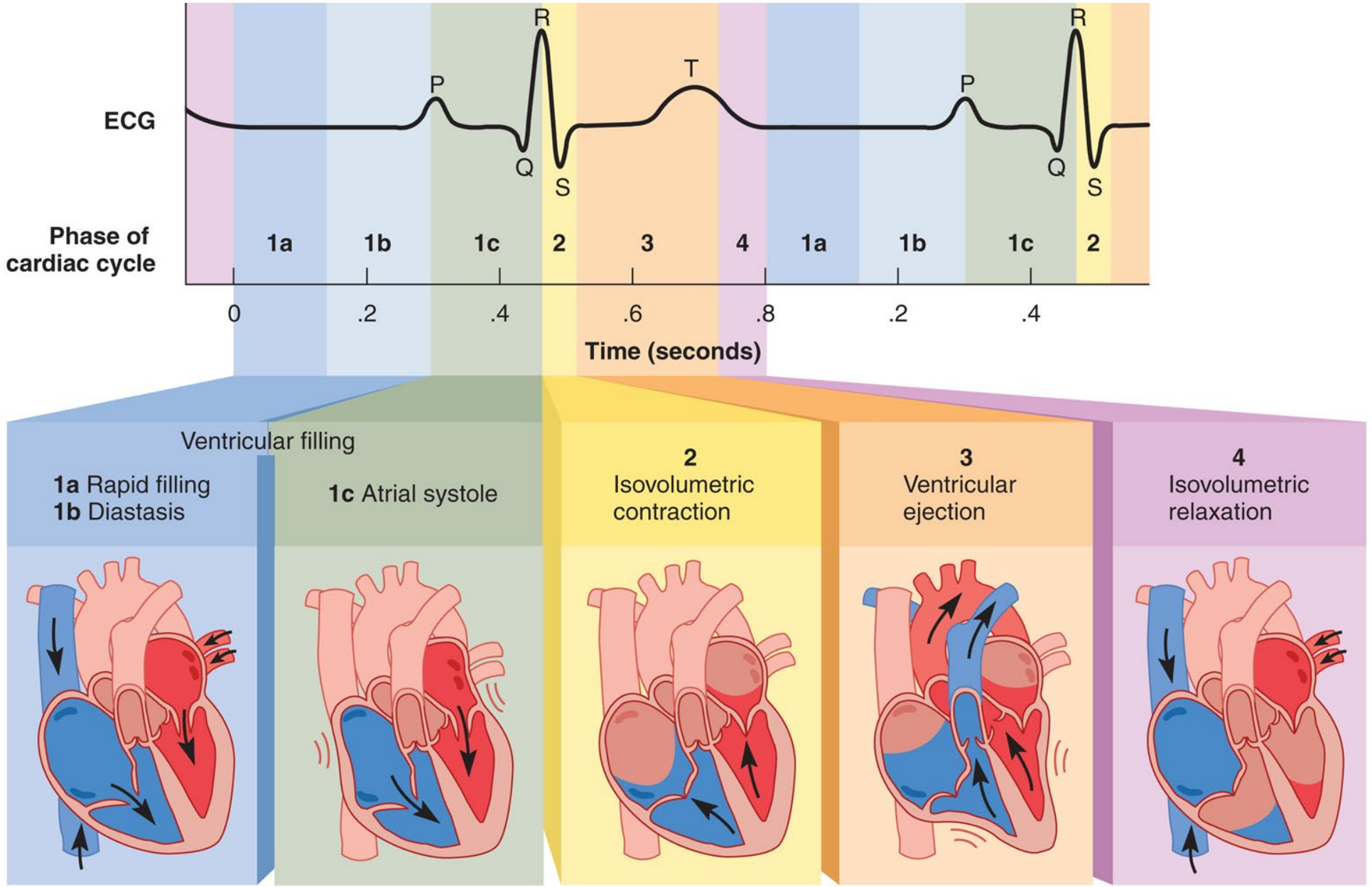
Ejection fraction of about 54% /// as high as 90% in vigorous exercise

The long prolonged contraction of ventricles associated with slow calcium channels // the plateau of the myocardiocyte action potential

End-systolic volume (ESV) // 60 mL of blood left behind

T wave occurs at the end of this phase (end systolic volume phase) as ventricles repolarize and then enter diastole

Events of Ventricular Ejection



Isovolumetric Relaxation

All four valves are closed.

Occurs during early ventricular diastole /// when T wave ends and the ventricles enter diastole (muscle relaxes)

Diastole of ventricles cause pressure to drop in ventricles

Due to elastic recoil from blood inside the aorta and pulmonary truck /// blood now moves towards the ventricles

This reverse flow of blood fill the “cusps” of the semilunar valves and close the semilunar valves

Creates a slight pressure rebound that appears as the **dicrotic notch** of the aortic pressure curve

AV valves are still closed because pressure in ventricles are still greater than the pressure in the atria – all four valves are closed

This is isovolumetric relaxation! And all four valves are closed.

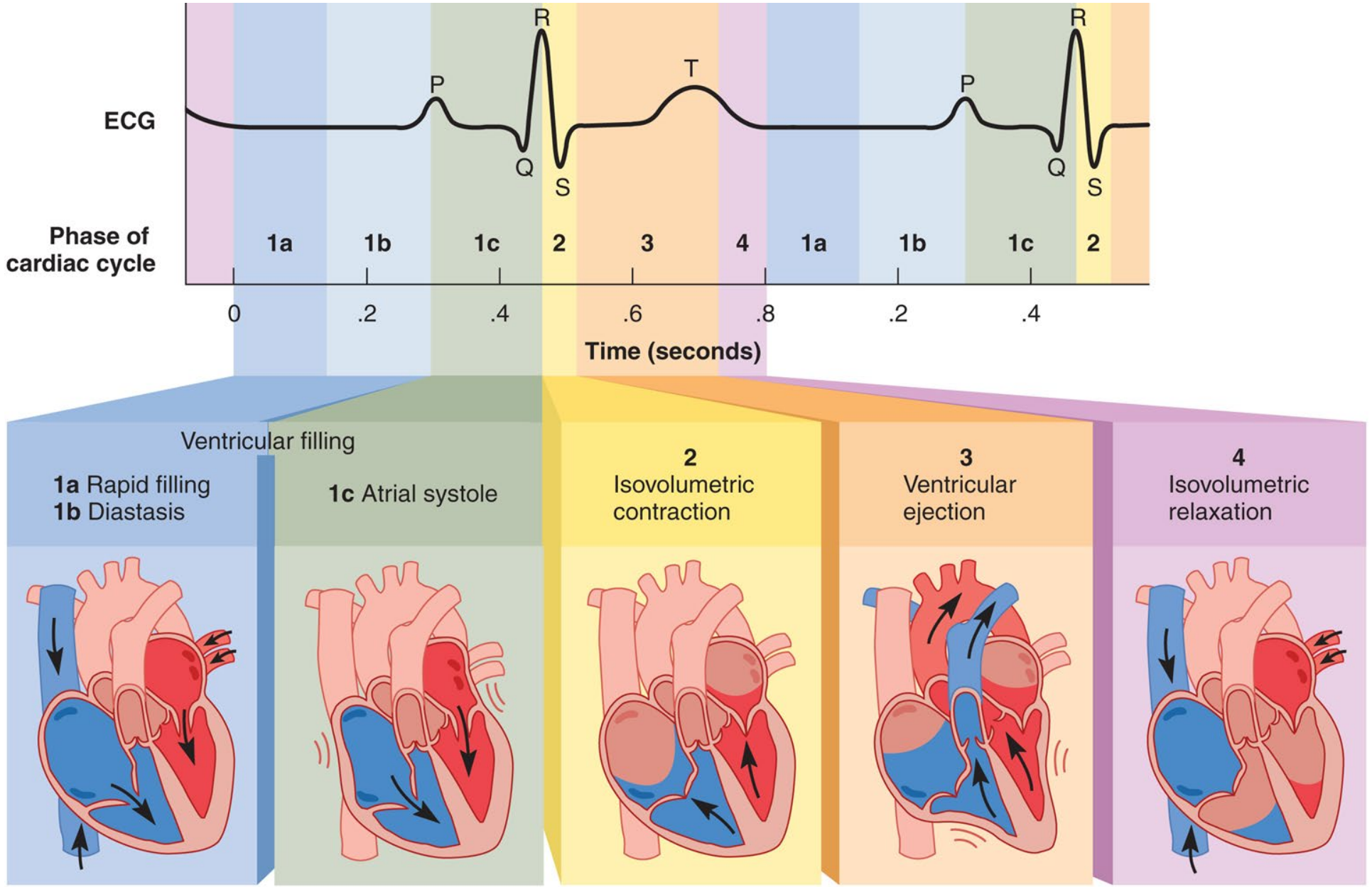
Sound at Start of Isovolumetric Relaxation

Heart sound S_2 occurs as blood closes semilunar valves

AV valves are also closed at this time, so ventricles are unable to receive blood

When pressure in atria exceed ventricluar pressure then AV valves open again to renew ventricular filling

Isovolumetric Relaxation

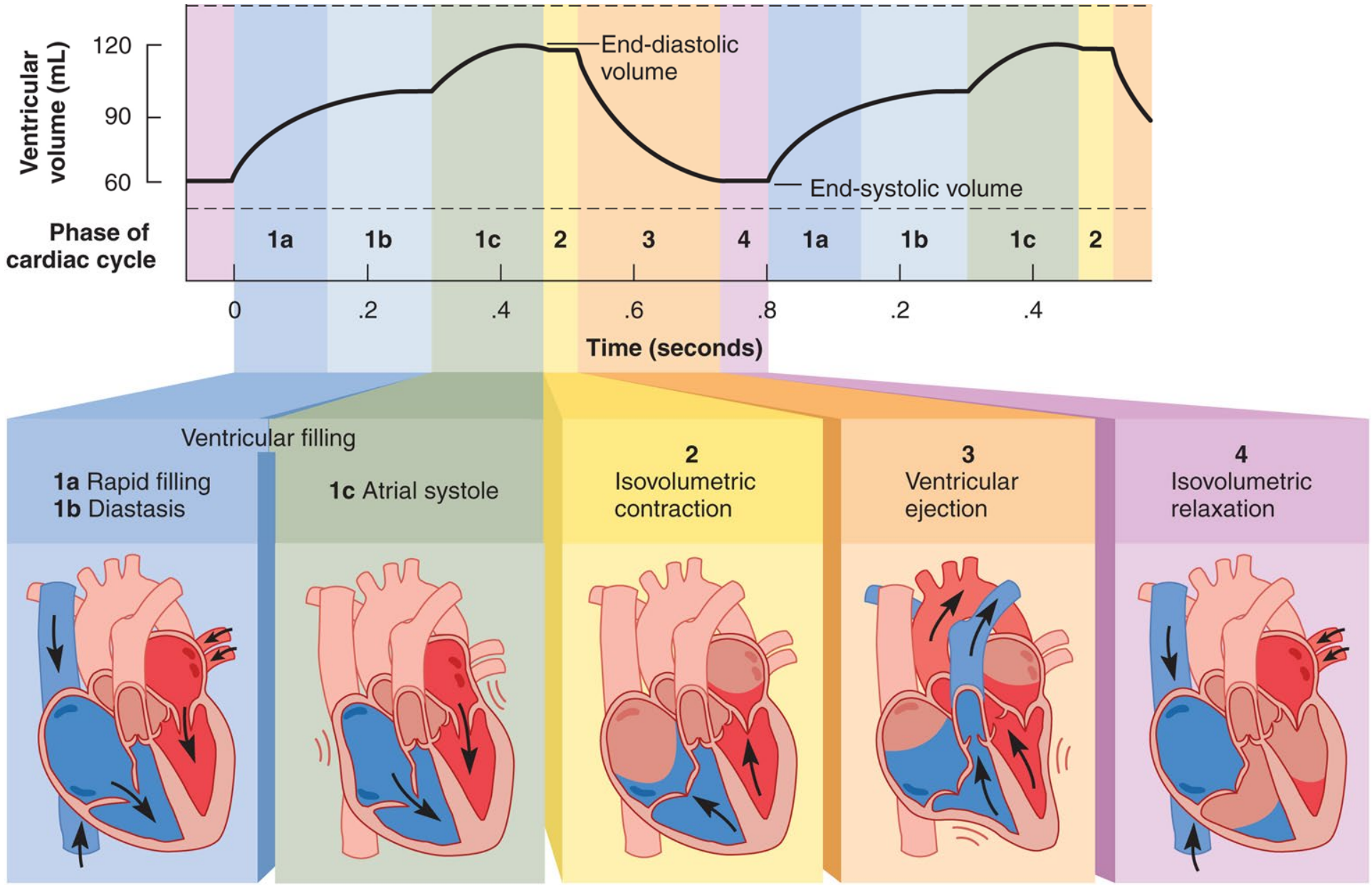


Overview of Volume Changes

end-systolic volume (ESV)	60 ml
passively added to ESV during atrial diastole	30 ml
added to ESV by atrial systole	40 ml
Total end-diastolic volume (EDV)	130 ml
stroke volume (SV) / blood ejected	
ejected by ventricular systole	-70 ml
end-systolic volume (ESV)	60 ml

- *Both ventricles must eject same amount of blood*
- *Volume is the same, but pressure is different*

Overview of Volume Changes



Heart Sounds

Auscultation - listening to sounds made by body

First heart sound (S_1), louder and longer “lubb”, occurs with closure of AV valves, turbulence in the bloodstream, and movements of the heart wall

Second heart sound (S_2), softer and sharper “dupp” occurs with closure of semilunar valves, turbulence in the bloodstream, and movements of the heart wall

S_3 - rarely heard in people over 30

Pressure Gradients / Blood Flow / Valve Function

Fluid flows only if it is subject to a pressure gradient /// fluid flows down a pressure gradient from high pressure to low pressure

Follow events that occur on left side of heart (note: similar events occur on the right side of the heart but with lower blood pressure / left and right heart functions must occur simultaneously)

When ventricle relaxes and expands (this allows ventricles to fill with blood (this is pre-load in ventricle) // occurs as ventricle internal pressure falls

If bicuspid valve is open, blood flows into left ventricle

When ventricle starts to contract, pressure increases - blood flow towards atria / this closes AV valves (What prevents prolapse?)

After AV valves closes, pressure in ventricle continues to rise // the aortic valve is now pushed open (overcoming after-load = the pressure above semilunar valves in plumonary truck and aorta) /// when afterload pressure is exceeded in ventricles, blood is ejected blood flows into aorta

Cardiac Output = stroke volume X heart rate

CO about 4 to 6 L/min at rest (test figure 5.25 L per min)

This means a RBC leaving the left ventricle will arrive back at the left ventricle in 1 minute (approximately 5.25 L of blood in circulation)

Vigorous exercise increases CO during event

Fit person up to 21 L/min

World class athlete up to 35 L/min

Cardiac reserve – the difference between a person's maximum and resting Cardiac Output

Two Factors Influence Cardiac Output

Cardiac output = stroke volume x heart rate

Volume of blood ejected by ventricles in 1 minute

CO = 70 ml / Beat x 75 Beat / Minutes = 5.25 L / Min

Cardiac Output May Be Changed By

Chronotropic Effects (time // related to the heart rate)

Inotropic Effects (related to contraction force called contractility // increase contractility will increase stroke volume)

Heart Rate and Cardiac Output

Heart rate varies throughout life

- infants have HR of 120 bpm or more
- young adult females avg. 72 - 80 bpm
- young adult males avg. 64 to 72 bpm
- heart rate rises again in the elderly

- Positive chronotropic agents – factors that raise the heart rate
- Negative chronotropic agents – factors that lower heart rate

- Positive inotropic agents – factors that increase force of contraction
- Negative inotropic agents – factors that decrease force of contraction

Why is it important to maintain CO constant when at rest but increase CO when exercising?

- *When at rest, CO is "regulated" so CO = 5.25 L / min /// Why?*
- *Therefore, if at rest and stroke volume increases due to conditioning, then HR will fall*
- *Stoke volume increases with exercise because ventricle hypertrophy and increase in contractility*
- *This means the heart is not working as "fast" /// therefore it may "last longer"!!!!*
- SV increases with fitness /// SV decreases with disease and aging

To keep cardiac output constant as we increase in age, the heart rate increases as the stroke volume decreases

cardiac output = stroke volume x heart rate

The other factor that influence cardiac output

Three variables govern stroke volume:

Preload (more preload = more SV = more blood ejected!)

After load (blood pressure in aorta which resist ejection of blood from heart) /// if afterload increases there is more resistance to eject blood / result in less SV)

Contractility = inotropic influence = as force of myocardiocyte contraction increases results in more SV

Net result:

- increased preload or increasing the contractility increases stroke volume
- increased after load causes decrease stroke volume

Preload and Stroke Volume

Preload – the amount of tension (caused by filling of the ventricles) in myocardium immediately before it begins to contract

As you Increase preload you increase force of contraction

Exercise increases venous return, preload, and stretches myocardium

Cardiocytes generate more tension (not like skeletal muscle / no tension length relationship)

Increased cardiac output matched to increased venous return

Frank-Starling Law of the Heart - SV$\propto$ EDV

- –stroke volume is proportional to the end diastolic volume
- –ventricles eject as much blood as they receive
- –the more they are stretched, the harder they contract // not like skeletal muscle

Afterload and Stroke Volume

After load – the blood pressure in the aorta and pulmonary trunk "above" their semilunar valves

After load prevents the aortic and pulmonary semilunar valves from opening

You must overcome afterload to eject blood

After load limits stroke volume

Hypertension increases after load and opposes ventricular ejection // overtime cause hypertrophy of heart // enlarged heart is very bad!

What causes cor pulmonale?

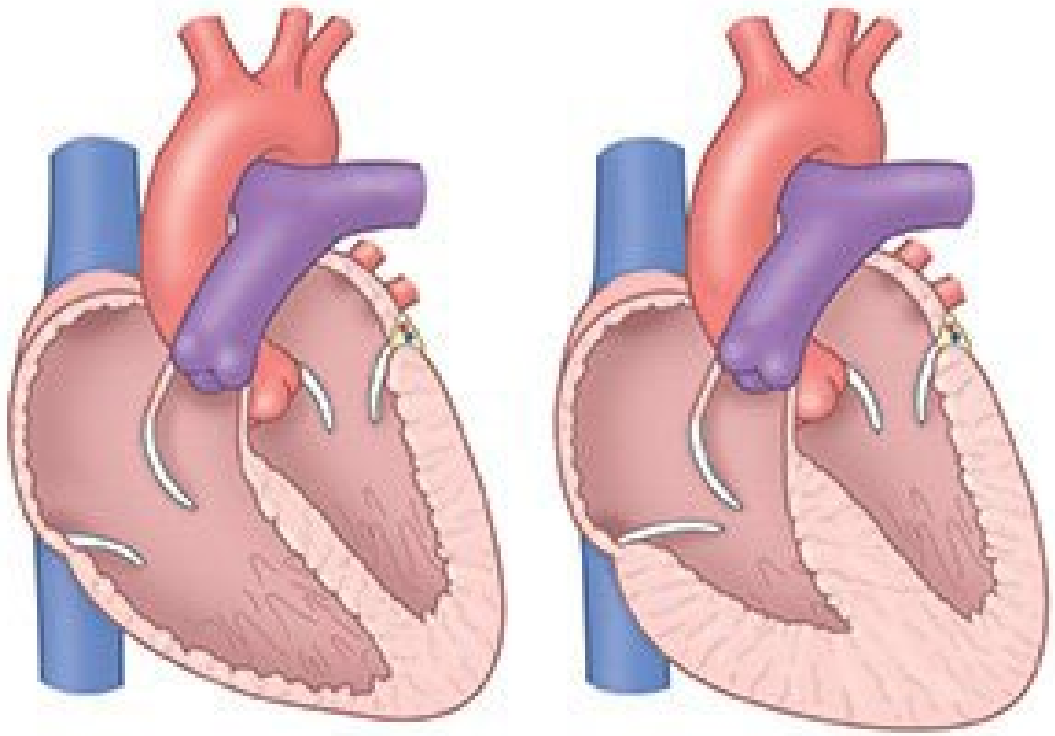
Anything that *impedes circulation* in either the systemic or pulmonary circuit may also increase after load (pressure above semilunar valve)

Lung diseases will restrict blood flow into pulmonary circulation // blood "backs up" /// pressure "builds up" above the pulmonary semilunar valve

Cor pulmonale – results in right ventricular failure due to *obstructed pulmonary circulation // right ventricular wall hypertrophy*

These diseases *obstruct pulmonary circulation* through lungs: emphysema, chronic bronchitis, and black lung disease

Cor Pulmonale



Normal

Right ventricular hypertrophy

Inotropic VS Chronotropic Factors

Positive inotropic agents that increase contractility

Hypercalcemia can cause strong, prolonged contractions and even cardiac arrest in systole

Catecholamines increase calcium levels

Glucagon stimulates cAMP production

Digitalis raises intracellular calcium levels and contraction strength

Inotropic VS Chronotropic

Negative inotropic agents reduce contractility

Hypocalcemia can cause weak, irregular heartbeat and cardiac arrest in diastole

Hyperkalemia reduces strength of myocardial action potentials and the release of Ca^{2+} into the sarcoplasm

Vagus nerve has an effect on atria (the nodes) which reduces heart rate

However…..few vagus nerves innervate myocardiocytes in ventricles /// therefore vagus has no significant negative inotropic effect

Chronotropic Effects of the Autonomic Nervous System

Autonomic nervous system does not initiate the heartbeat,

ANS modulates the rhythm and force

- Cardiostimulatory effect - some neurons of the cardiac center transmit signals to the heart by way of sympathetic pathways

- Cardioinhibitory effect - others transmit parasympathetic signals by way of the vagus nerve

Chronotropic Effects of the Autonomic Nervous System

Sympathetic postganglionic fibers are adrenergic

They release norepinephrine // binds to β-adrenergic receptors in the heart

Activates c-AMP second-messenger system in *cardiocytes (and nodal cells) --- result in 3 important events*

- Leads to the opening of slow Ca^{2+} channels in plasma membrane / fibers contract more quickly
- Opens calcium channels in sarcoplasmic reticulum / fibers contract more quickly
- cAMP accelerates the uptake of Ca^{2+} by the sarcoplasmic reticulum // fibers relax more quickly

Net result is ability to accelerate heart rate up to 240 bpm!

Chronotropic Effects of the Autonomic Nervous System

Parasympathetic (vagus nerves) are cholinergic fibers // inhibitory effects on the SA and AV nodes

Acetylcholine (ACh) binds to muscarinic receptors (these are metabotropic second messenger type receptors using G-proteins to make cAMP that then opens up a third transmembrane protein channel)

Ach opens K^+ gates in the nodal cells

As K^+ leaves the cells, they become hyperpolarized and fire less frequently

Heart slows down

The parasympathetic effect on the heart is faster acting than the sympathetic effect

Chronotropic Effects of the Autonomic Nervous System

Vagal Tone (parasympathetic tone)

The heart has an intrinsic “natural” firing rate of 100 bpm

This means if both sympathetic and parasympathetic fibers are cut going to the SA node then the heart rate is faster!!!! why?

Because the heart is under vagal tone – holds down this natural heart rate to 70 – 80 bpm at rest /// caused by steady background firing rate of the vagus nerves

Chronotropic Chemicals

Chemicals may affect heart rate // in addition to the neurotransmitters from cardiac nerves

Blood born adrenal catecholamines (NE and epinephrine) are potent cardiac stimulants

Drugs that stimulate the heart

nicotine stimulates catecholamine secretion from adrenal gland

thyroid hormone increases number adrenergic receptors on heart so more responsive to sympathetic stimulation

caffeine inhibits cAMP breakdown /// therefore can prolong the adrenergic effect

Potassium Chronotropic Effect

Electrolyte : K^+ the has greatest chronotropic effect

Hyperkalemia (higher than normal concentration in blood)

–Result / to much K^+ diffuses into cardiocytes / non excess K^+ cytoplasm
–Membrane voltage elevated // now resting potential closer to threshold
–As K concentration increases sodium leaking channels down regulated
–Repolarization harder to achieve
–Myocardium becomes less excitable
–Heart rate slows and becomes irregular
–May *arrest in diastolic phase*

Potassium imbalances are very dangerous and require emergency medical treatment!

What may happen after a crush injury to the arm?

Potassium Chronotropic Effect

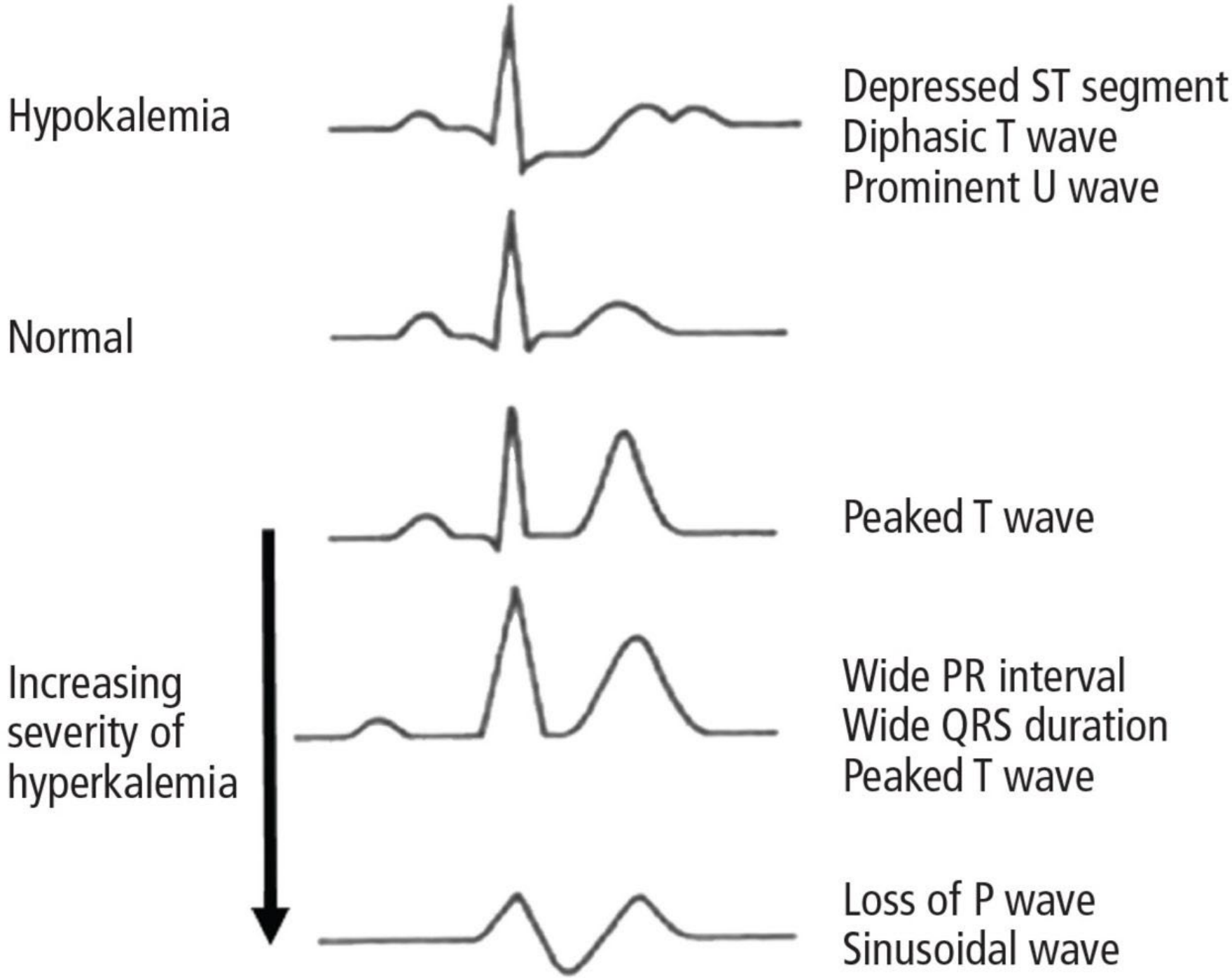
Electrolyte : K^+ the has greatest chronotropic effect

Hypokalemia (lower than normal concentration in blood)

K^+ diffuses out of the cardiocytes

Cells hyperpolarized / membrane potential more negative

Require increased stimulation to reach threshold / harder to stimulate heart


Hypokalemia
Depressed ST segment
Diphasic T wave
Prominent U wave
Normal
Peaked T wave
Increasing severity of hyperkalemia
Wide PR interval
Wide QRS duration
Peaked T wave
Loss of P wave
Sinusoidal wave

Chronotropic Effects of Electrolytes

Electrolyte : Ca^{2+} also affect heart rate (greater effect on contraction strength)

Hypercalcemia – excess of Ca^{2+}

–decreases heart rate and contraction strength

–slow heart rate

Hypocalcemia – deficiency of Ca^{2+}

–increases heart rate

–rare condition

–greater effect is on nerve fibers causing action potential in somatic nerve fibers going to skeletal muscles (like diaphragm) / more likely to cause death from respiratory arrest!

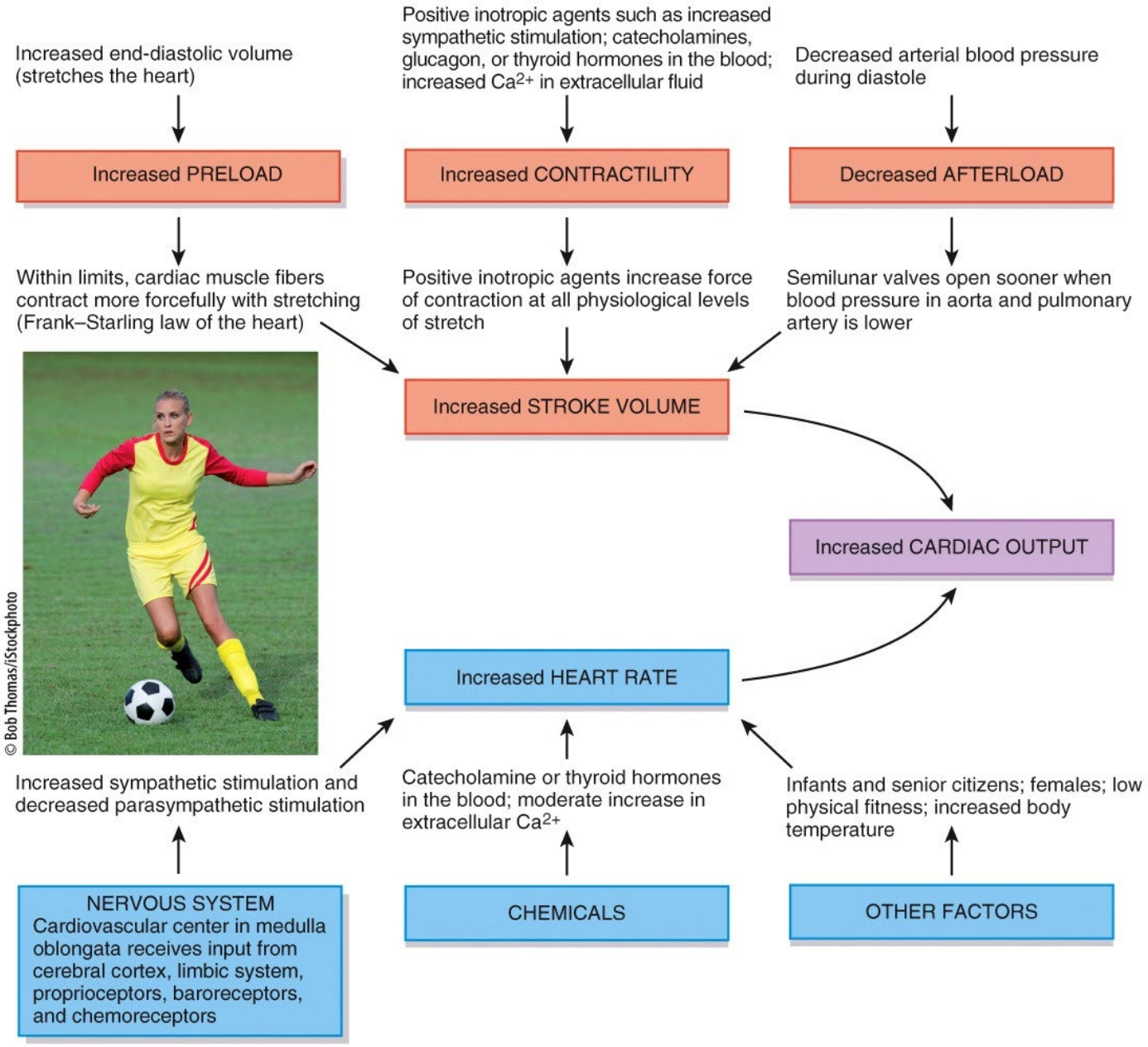
Why May Extreme Chronotropic Effects Reduce Stroke Volume?

By accelerating the rate of contraction (how fast calcium is added to sarcoplasm) and then accelerating the reuptake of calcium into sarcoplasmic reticulum to increase rate of relaxation --- heart rate is increased!

Sympathetic NS (norepinephrine) able to increase the heart rate as high as 240 bpm

At 240 bpm both stroke volume and cardiac output are reduced

Why? Note: at these high heart rates / diastole becomes too brief for complete filling of the ventricles!!!!



Great slide! Study this to learn key events.

Heart Function Terms

Pulse pressure – surge of pressure produced by each heart beat that can be felt by palpating a superficial artery with the fingertips

Tachycardia - resting adult heart rate above 100 bpm

stress, anxiety, drugs, heart disease, or fever

loss of blood or damage to myocardium

Bradycardia - resting adult heart rate of less than 60 bpm

in sleep, low body temperature, and endurance trained athletes

Exercise and Cardiac Output

- *Exercise improves heart functon*
- *Exercise will strengthen the heart resulting in an increase stroke volume*
- *Then heart rate can be slower and still reach target cardiac output (5.25 L/min)*
- *This will now increase cardiac reserve*
- Exercise stimulate proprioceptors in skeletal muscles that send signal to cardiac center

–at beginning of exercise, signals from joints and muscles reach the cardiac center
–sympathetic output from cardiac center increases cardiac output
–increased muscular activity /// increases venous return // increases preload /// results in an increase cardiac output

Increases in heart rate and stroke volume will both cause an increase in cardiac output

Exercise and Cardiac Output

Exercise will cause moderate ventricular hypertrophy

Result = increased stroke volume /// will allow heart to beat more slowly while at rest

This increases cardiac reserve in the athlete so they can tolerate more exertion during performance than a sedentary person

Note: a condition that causes a "pathologic enlarged heart" will reduce total ventricular volume and stroke volume. This then decreases CO. Therefore, heart rate will need to increase to keep CO at 5.25 L/min // more stress on heart

Valvular Insufficiency

Valvular insufficiency (incompetence) // any failure of a valve to prevent reflux (regurgitation) the backward flow of blood

Valvular stenosis – cusps are stiffened and opening is constricted by scar tissue

May result of **rheumatic fever** /// autoimmune attack on the mitral and aortic valves

Heart now overworked and may become enlarged

Valvular Insufficiency

Heart murmur – abnormal heart sound produced by regurgitation of blood through incompetent valves

Mitral valve prolapse – insufficiency in which one or both mitral valve cusps bulge into atria during ventricular contraction

hereditary in 1 out of 40 people /// may cause chest pain and shortness of breath

Congestive Heart Failure

The circulatory system is a closed system. The amount of blood ejected must be the same volume as blood returning.

Veins function as a blood reservoir so when we exercise total cardiac output increases in part because more blood is being moved from this venous reservoir.

CHF occurs when one ventricle ejects less than the its normal volume of blood. While the other ventricle ejects the proper amount of blood.

The ventricle which ejects less blood is the failing ventricle

Ventricular failure usually due to a heart weakened by

- myocardial infarction
- chronic hypertension
- valvular insufficiency
- congenital defects in heart structure.

Left Ventricular Congestive Heart Failure

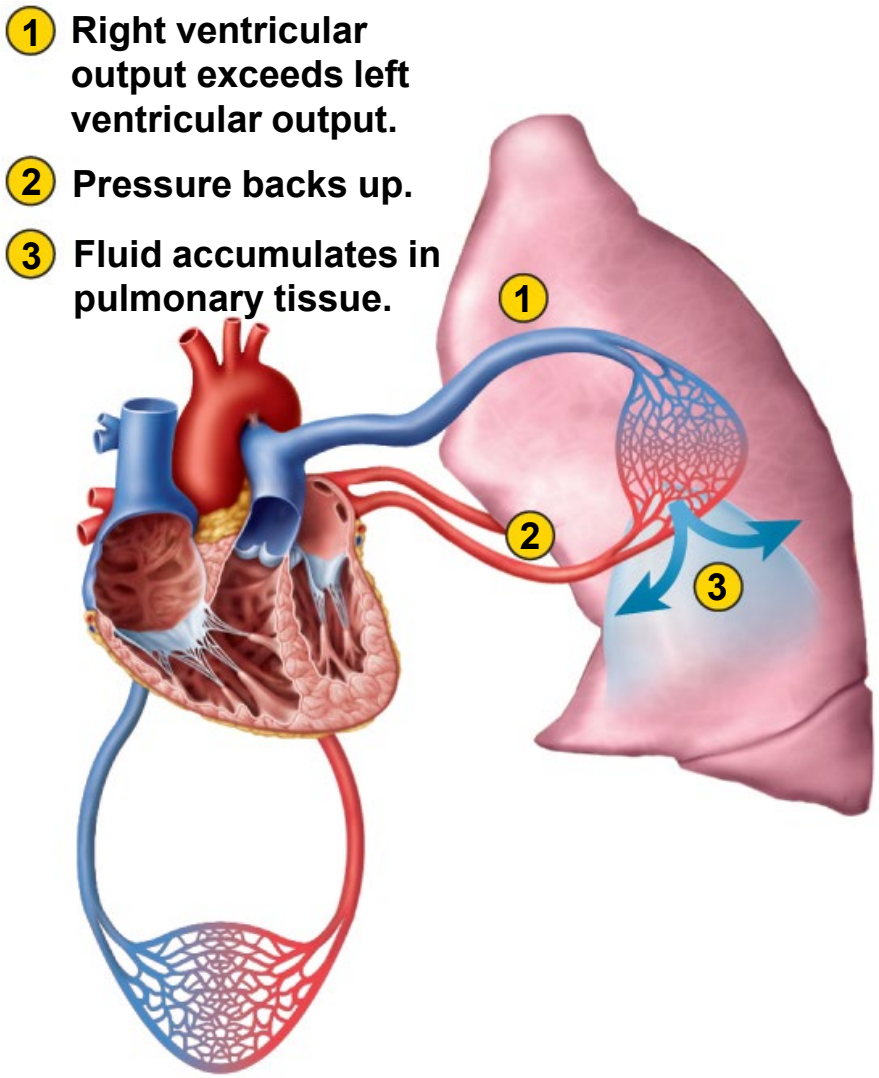
Left ventricle ejects less blood (e.g. Rt V ejects 70 ml and Lt V ejects 50 ml)

Right ventricle is ejecting 20 ml of blood more than the left ventricle with each cardiac cycle.

Extra “20 ml” of blood most go somewhere but can not return to the left ventricle // extra 20 ml must accumulate in the lung interstitial space // pulmonary edema

–Shortness of breath and sense of suffocation

Unbalanced Left Ventricular Output



(a) Pulmonary edema

Left ventricular failure results in pulmonary edema

Note:

Cor pulmonale will also results in pulmonary edema

Due to lung emphysema and other disease states which cause restriction (fibrosis) in lung tissue

Enlarged right heart // these condition will contribute to right heart failure

Right Ventricular Congestive Heart Failure

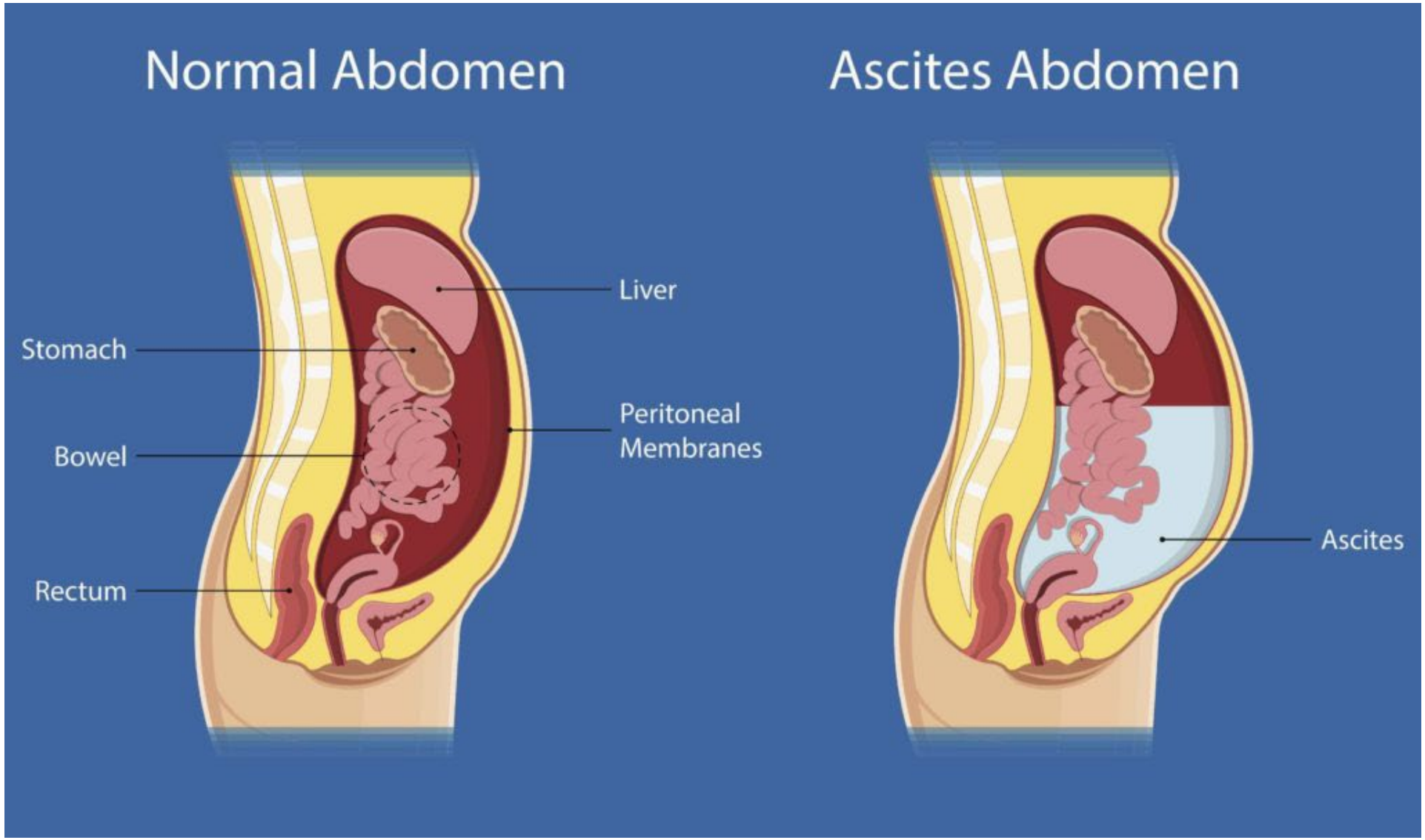
Right ventricle ejects less blood (e.g. Lt V ejects 70 ml and Rt V ejects 50 ml)

Left ventricle ejects extra 20 ml of blood per cardiac cycle

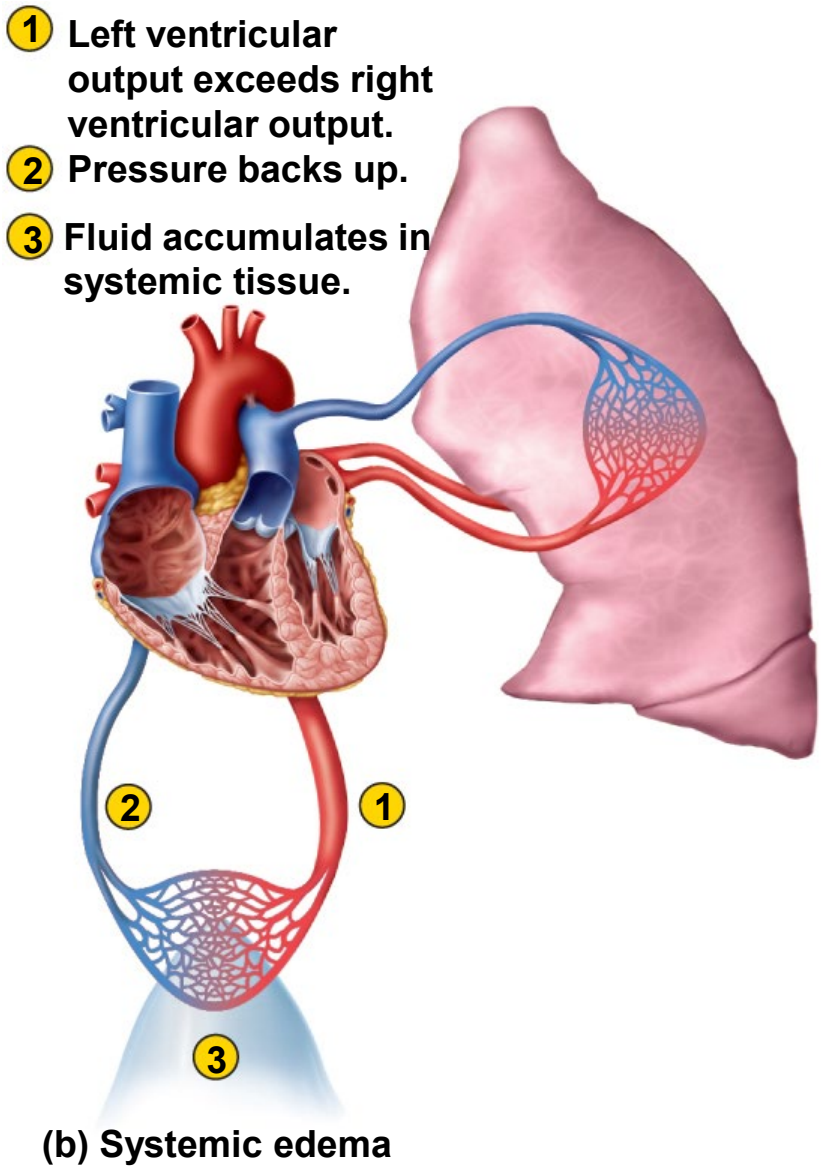
Rt ventricle can not receive the total volume so extra 20 ml filters into the systemic interstitial space // systemic edema - seen primarily in the legs

Enlargement of the liver, ascites (pooling of fluid in abdominal cavity), distension of jugular veins, swelling of the fingers, legs, ankles, and feet

- *Note: Both imbalance in right and left ventricular ejection is a condition that will eventually lead to total heart failure*


Normal Abdomen
Liver
Stomach
Peritoneal
Membranes
Bowel
Rectum
Ascites Abdomen
Ascites

Unbalanced Right Ventricular Output



(b) Systemic edema

Right ventricular failure results in systemic edema

Fluid accumulates in legs, abdominal cavity, enlarged liver.

Shock – Loss of Blood Pressure

Hypovolumic
- Hemorrhage
- Loss of blood
- Loss of blood pressure

Cardiac Shock
- Lower heart rate
- Falling blood pressure

Neurogenic Shock
- Decrease in sympathetic tone to arterioles
- Arteriole dilation
- Falling blood pressure
- Anaphylactic shock – antigen causes systemic basophile degra

Shock

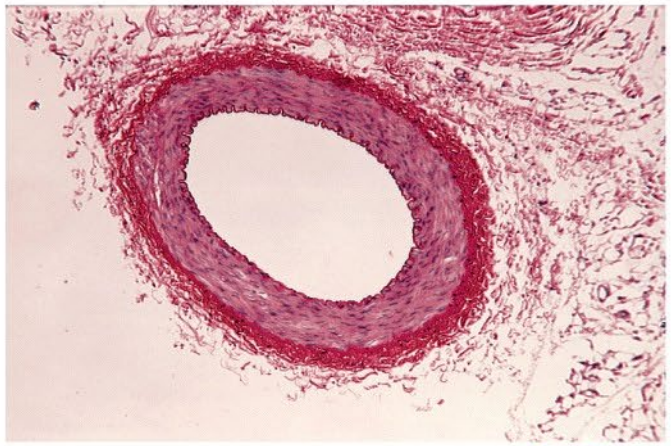
Compensated Shock
- Increase blood pressure
- Increase respiration
- Constriction of arterioles
- Pale cool skin

Decompensated Shock
- Low blood pressure
- Lack of perfusion
- Falling blood pressure

Irreversible Shock
- Perfusion to organs can not be restored
- Cell damage / death
- Organ damage / death

Pathology in Heart's Arteries

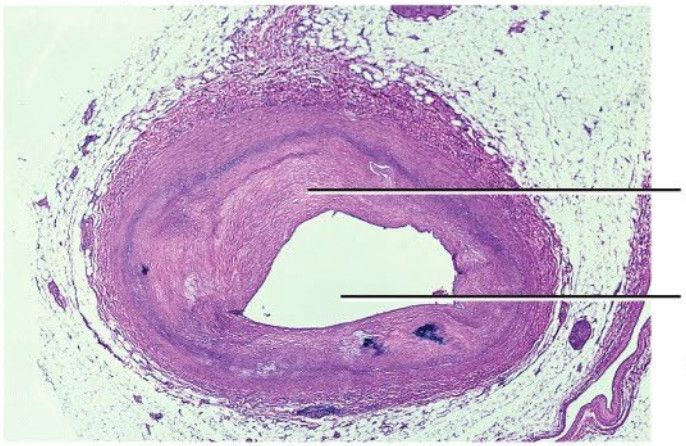
Chuck Brown/Photo Researchers, Inc.



LM 16x

Normal artery

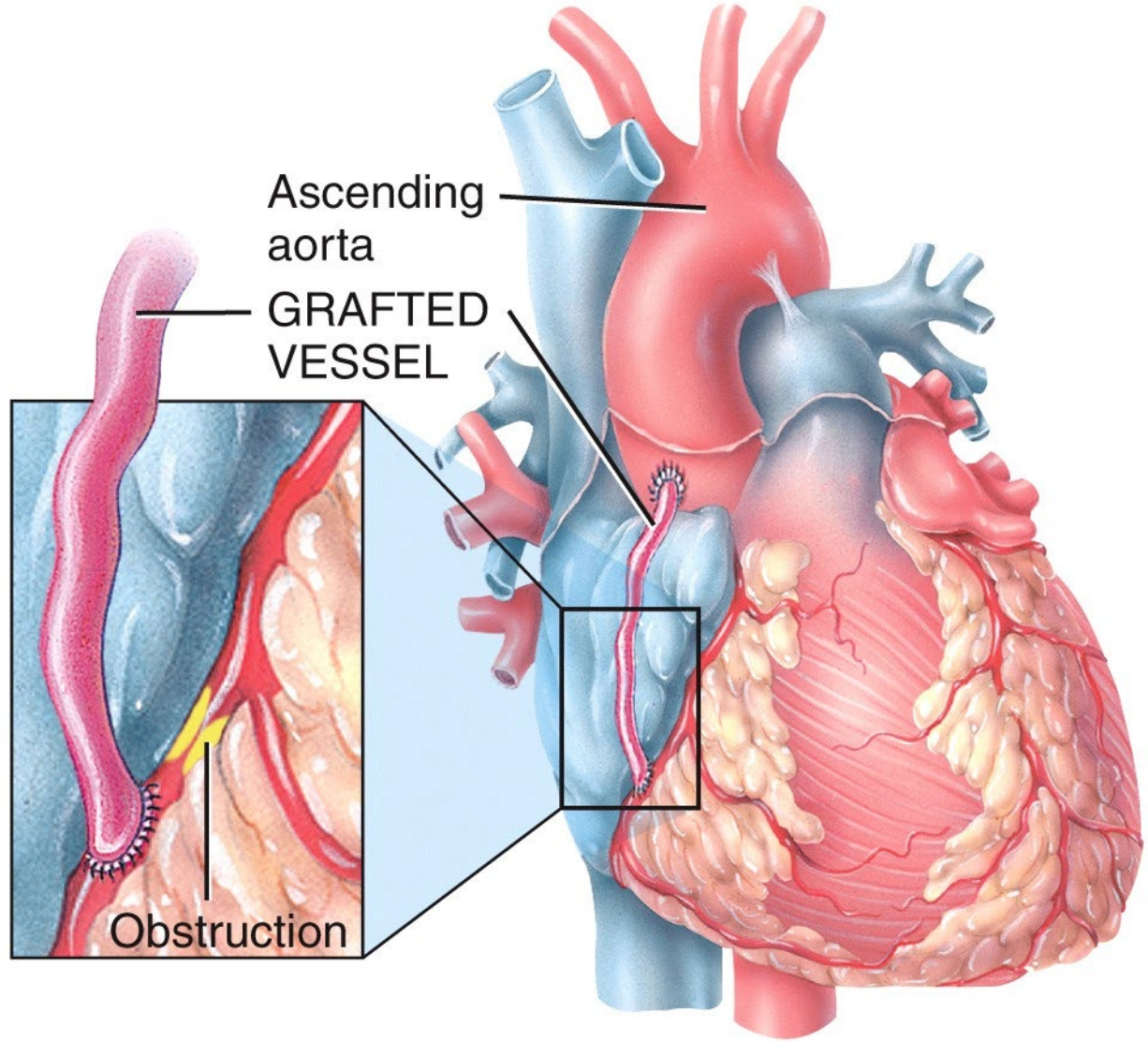
Carolina Biological Supply Company/Phototake



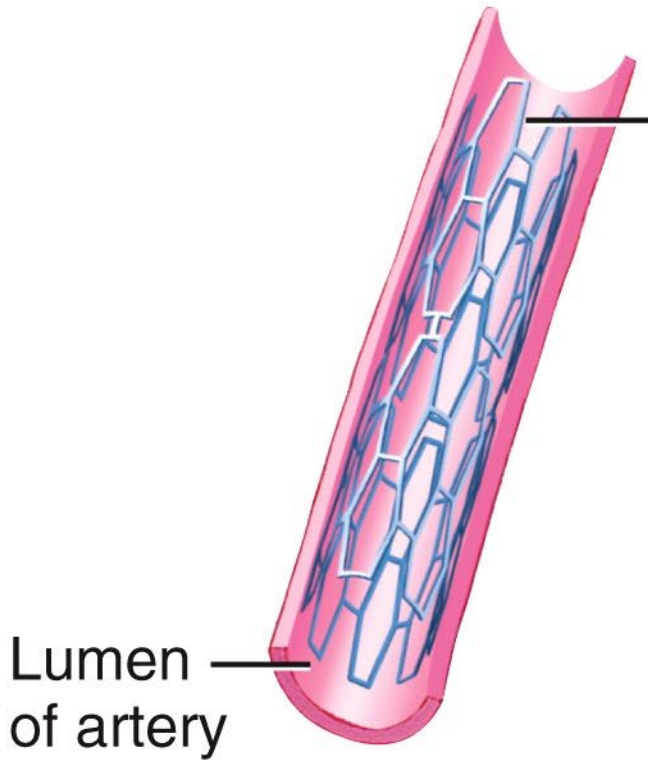
LM 20x

Obstructed artery

What is arteriosclerosis?



(a) Coronary artery bypass grafting (CABG)



(c) Stent in an artery

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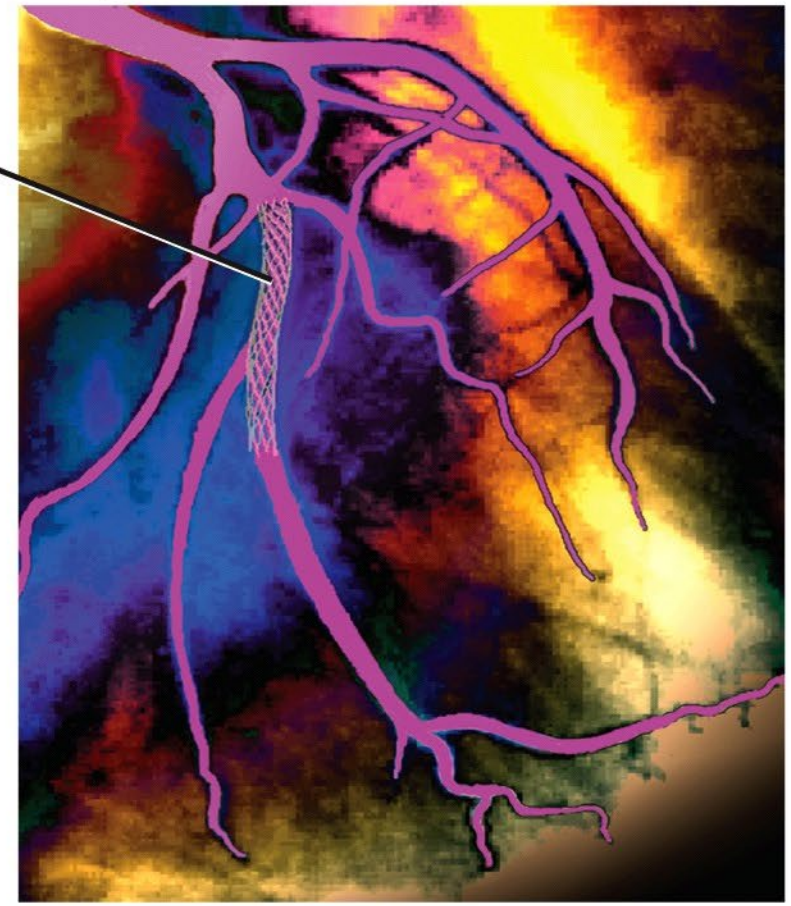

(d) Angiogram showing a stent in the circumflex artery